Ten years of METEOR (an international rheumatoid arthritis registry): development, research opportunities and future perspectives

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ABSTRACT

Objective. *Ten years ago, the METEOR tool was developed to simulate treatment-to-target and create an international research database. The development of the METEOR tool and database, research opportunities and future perspectives are described.*

Methods. *The METEOR tool is a free, online, internationally available tool in which daily practice visits of all rheumatoid arthritis patients visiting a rheumatologist can be registered. In the tool, disease characteristics, patient- and physician-reported outcomes and prescribed treatment could be entered. These can be subsequently displayed in powerful graphics, facilitating treatment decisions and patient-physician interactions. An upload facility is also available, by which data from local electronic health record systems or registries can be integrated into the METEOR database. This is currently being actively used in, among other countries, the Netherlands, Portugal and India.*

Results. *Since an increasing number of hospitals use electronic health record systems, the upload facility is being actively used by an increasing number of sites, enabling them to benefit from the benchmark and research opportunities of METEOR. Enabling a connection between local registries and METEOR is a well established but time-consuming process for which an IT-specialist of METEOR and the local registry are necessary. However, once this process has been finished, data can be uploaded regularly and relatively easily according to a pre-specified format. The METEOR database currently contains data from >39,000 patients and >200,000 visits, from 32 different countries and is ever increasing. Continuous efforts are being undertaken to increase the quality of data in the database.*

Conclusion. *Since METEOR was founded 10 years ago, many rheumatologists worldwide have used the METEOR tool to follow-up their patients and improve the quality of care they provide to their patients. Combined with uploaded data, this has led to an extensive growth of the database. It now offers a unique opportunity to study daily practice care and to perform research regarding cross-country differences in a large, worldwide setting, which could provide important knowledge about disease and its treatment in different geographic and clinical settings.*

Introduction

Treat-to-target has been repeatedly shown to be highly effective in rapidly reducing disease activity in rheumatoid arthritis (RA) patients (1). Such treat-to-target strategy requires a long-term follow-up of patients with regular assessments of treatment effectiveness, using validated disease activity measures such as the Disease Activity Score (2) (DAS), the Simplified Disease Activity Index (3) (SDAI) or the Composite Disease Activity Index (4) (CDAI). Although highly effective, treat-to-target is not always followed in clinical practice (5), possibly because it is not always easy to obtain a fast disease activity measurement. Therefore 10 years ago, in 2006, the Measurement of Efficacy of Treatment in the "Era of Outcome" in Rheumatology (METEOR) tool was developed to stimulate treat-to-target, improve patient care and create an international RA research database (6).

The METEOR tool

The METEOR tool is a free, online tool available worldwide in different languages. The tool is entirely web-based and easy to use and can therefore

be used without involvement of the local IT department. Within each centre using METEOR, one coordinator (*e.g.* a rheumatologist or research nurse) is appointed and receives administrator rights from the METEOR organisation. This administrator can create all user accounts necessary for that centre. All METEOR users within each centre can access the METEOR tool with their own account and can at the same time access all patient data entered by their colleague users in the same centre. This easy implementation strategy has facilitated worldwide spread of the METEOR tool.

In the tool, the data of all RA patients visiting a rheumatologist can be entered. This can be new as well as existing RA patients, who are followed according to usual care. Each visit of the patient can be registered in METEOR. In 7 structured screens within the tool, data about patient and disease characteristics, patient and physician reported outcomes and prescribed treatment could be registered (Table I). Based on the available data, the tool automatically calculates a range of disease activity scores: DAS, DAS-3 (DAS calculated with 3 components), DAS28 (DAS based on 28-joint count), DAS28-3 (DAS based on 28-joint count and 3 components), SDAI, CDAI and Routine Assessment of Patient Index Data (RAPID3) (7). Medications, disease activity and physical functioning are subsequently displayed in illustrative and user-friendly graphics, facilitating treatment decisions and patient-physician interactions. The METEOR tool also offers benchmarking possibilities, to compare patient data, care indicators and treatment at the level of the rheumatologist, site, country or the complete METEOR database. Furthermore, it is possible to provide limited user access to patients, such that patients can complete the HAQ(8) at home prior to the consultation, in order to enhance the quality of the consultation.

Data protection and safety

All patient data in the METEOR database are anonymised, by storing all patient identifying data in an encrypted manner. Therefore, for none of the included countries – *e.g.* the Netherlands, Portugal, South Africa, Mexico and the USA – an informed consent is needed when adding new patients to the database. Identifying data can only be decrypted by the site that has created the data, such that rheumatologists always have access to detailed data regarding their own patients. Since the METEOR database contains medical data, it is impossible to delete data. Instead, data may be invalidated in case of errors, such that new and correct data may be created. A yearly check is performed to ensure that data protection and safety are in accordance with data protection regulations of all included countries.

Upload and download facilities

In recent years, an increasing number of hospitals have implemented Electronic Health Records (EHR) to record daily patient care. This means that using METEOR as a separate tool necessitates double data entry, thereby costing instead of saving time for the physician. In order to overcome the burden of double data entry, METEOR has developed upload and download facilities. With the download facility, data from the METEOR database can be uploaded in the local EHR system. The upload facility can be used to upload data from the local EHR system into the METEOR database, but it can also be used to link data from local databases to the METEOR database. The upload facility is currently being actively used in, among other countries, the Netherlands, Portugal (9) and India. Using the upload or download facilities enables users to benefit from the benchmark and research facilities, without the problem of double data entry or having to give up the local registries.

The METEOR database contains a total of 200 data elements, grouped in a complex structure of 7 tables. This structure ensures high speed data entry and data extraction for research purposes. It also allows for missing data, since tool users are not obliged to fill out all fields and it ensures internal consistency of the database. However, it also results in a very specific structure that is needed before data can be uploaded into the database. In general, between 150 and 200 data elements must be integrated in the METEOR database via the upload file.

A standardised XML-file, together with a reference guide and additional documentation, have been developed, to convert data from local registries into the correct format for upload into the database. Data from the local registry must be extracted and stored in this XML-file before they can be uploaded. Since this process is rather complicated, a local IT-expert is needed, who can cooperate with a METEOR IT-expert in order to develop a standardised procedure for data extraction, conversion and upload. The completed XML-file may be uploaded in a testing environment for validation. During this validation procedure, the quality and internal consistency of the XML-file is tested, as well as the correct format of each item. Due to the complex database structure, the validation cannot be performed only

Table I. Variables collected in METEOR (adapted from van den Berg *et al*. [10], with permission).

Patient characteristics
Age
Gender
Marital status
Smoking habits
Height
Weight
Disease characteristics
Date of symptom onset
Date of diagnosis
Erosions (present/absent/unknown)
Rheumatoid factor (present/absent/unknown)
ACPA (present/absent/unknown)
Tender joint count (53 or 28)
Swollen joint count (44 or 28)
Ritchie Articular Index
Erythrocyte sedimentation rate levels
C-reactive protein levels
Comorbidities
Physician reported outcomes
Physician global disease activity
Patient-reported outcomes
Patient global disease activity
Visual analogue scale for pain
Health Assessment Questionnaire
RAPID3
Treatment
Drugs (type, dose, start and end date)
Intra-articular injections
Surgery

ACPA: anti-citrullinated protein antibodies; RAPID3: Routine Assessment of Patient Index Data.

Table II. Examples of research projects performed in the METEOR database (adapted from van den Berg *et al*. [10], with permission).

Topic	Aim	Conclusions
Patient's *versus* physician's global disease activity (11, 12)	To compare the differences between patient and physician global disease activity and identify factors that might influence these differences. In addition, to assess whether these differences vary across 13 countries.	Differences between patients and physician global disease activity vary across countries. In general, agreement between patient and physician was moderate. In most countries patients scored on average higher than physicians. Patients based their judgment primarily on pain, whereas rheumatologists based it on swollen joint count and ESR level.
DAS steered therapy in clinical practice (13)	To evaluate treatment adjustments in response to DAS in RA patients in clinical practice in one centre in the Netherlands.	The majority of patients assessed had already achieved low disease activity, reflecting appropriate treatment intensity. When DAS ≥2.4, treatment was often not intensified due to high tender joint count or specific treatment combinations. This suggests that while aiming for low DAS, physicians have an individual approach, weighting whether all DAS elements are consistent with the total DAS and weather individual variables are likely to respond to DMARD adjustment or not.
Obesity and disease activity (14)	Is BMI associated with RA disease outcomes?	In patients with established RA obesity was associated with higher DAS28 and reduced odds of achieving DAS28 remission. In early RA, obesity was not associated with adverse disease activity outcomes.
Is there an effect of treat-to-target training? (15)	To investigate if rheumatologists from several countries that report to agree with existing guidelines indeed follow them up in clinical practice.	Reporting to be compliant with EULAR recommendations and T2T principles, even after dedicated education, does not mean that rheumatologists actually comply with it in clinical practice.
TNF inhibitor use across countries (16)	To investigate whether the relative distribution of TNFi prescriptions for RA varies among countries with different healthcare systems, during two time periods.	The relative prescription of various TNFi differed significantly across several EU countries and the US. Infliximab was prescribed significantly more in EU countries compared to US sites in period 1 (2009-2010). In Italy and Portugal, etanercept was prescribed significantly more than other TNFi in period 2 (2011-2012).
Comparison of RA disease activity indices in two populations (17)	To assess disease activity states using DAS28, CDAI and SDAI and to compare their outcomes in two RA populations.	CDAI and SDAI classified approximately the same number of patients in remission in Portugal and the Netherlands. DAS28 classified a higher percentage of Dutch patients as being in remission, due to a lower ESR.
Quality indicators in RA in clinical practice (18)	To test the feasibility of collecting, storing, retrieving and analysing necessary information to fulfil a preliminary set of quality indicators that have been proposed by an international task force.	Most of the quality indicators that were proposed by the task force were feasible in clinical practice in most parts of the world.

ESR: erythrocyte sedimentation rate; DAS: Disease Activity Score; DMARD: disease-modifying anti-rheumatic drug; EULAR: European League Against Rheumatism; T2T: treat-to-target; RA: rheumatoid arthritis; TNF: TNF inhibitors; EU: European; US: United States; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index.

on a field-by-field level, but the correct relationship between fields also must be tested in order to lead to a consistent database. For example, not only the individual joint scores are stored, but also the complete DAS.

Whereas some items can be transferred directly from a local registry into METEOR, others require conversions. For example, medication data are often stored in different ways, which are not always consistent within one register. During the validation process, all possible errors and differences between the METEOR database and the register are identified, until all data can be uploaded in the correct format. When uncertainty still exists about the correctness of the data, these data are deleted, possibly leading to some missing values. According to experiences with already coupled registries, this is a relatively time-consuming process, requiring up to 5–10 subsequent attempts before all errors are eliminated. However, once this process has been completed, data from the XML-file can be relatively easily uploaded, according to the specified format. Then not only new data can be added to the database, but replacement of old data is also possible, in order to allow correction of erroneous data.

Research opportunities

All METEOR users who are actively contributing data to the database, including those centres that add data through the upload facility, can perform research in the database. The leading principle is that each participating rheumatologist or centre is the owner of its own data. Therefore, each user can at any time perform research using her/his own data. Researchers also may submit research proposals with a request to perform research on part of or the complete METEOR database. These research proposals are assessed by a scientific committee regarding relevance, quality and ethical aspects. Once approved by the scientific committee, a representative rheumatologist of each site can decide if they allow

their data to be used in that particular research project.

Currently, the METEOR database contains data from >39,000 patients and >200,000 visits, added by 78 sites using the METEOR tool and 50 sites using the upload facilities. These data stem from 32 different countries, which are ever increasing. Since rheumatologists are not obliged to complete all fields and sometimes technical issues exist when coupling local registries to the database, not all data are complete. Therefore, continuous efforts are being undertaken to increase the quality of the data in the database.

Nonetheless, the METEOR database offers unique research opportunities. Not only does its large size ensure a large statistical power to investigate an extensive variety of research questions. Furthermore, the strong international character of the database also offers a rare possibility to investigate cross-country differences. Although an increasing number of national databases exist, research questions regarding cross-country comparisons can be answered only by pooling information from these databases, which has already been performed in METEOR. Furthermore, since data are gathered in clinical practice, research questions regarding real life clinical practice can be answered. Some examples of research that has been performed in the METEOR database can be found in Table II.

Conclusions and future perspectives

The METEOR database was founded 10 years ago to stimulate treat-to-target, to improve patient care and to create an international RA research database. During these 10 years, many rheumatologists worldwide have started using the METEOR tool to follow-up their patients and to treat their patients more efficiently. Also, an increasing number of sites use the upload facilities to add data to the METEOR database, enabling them to benefit from the benchmark and research opportunities. This has led to the creation of a large international research database that offers a unique opportunity to study daily clinical practice and to perform research regarding cross-country differences. In the future, METEOR will continue to stimulate the worldwide use of the METEOR tool. Furthermore, in sites or countries in which EHRs are used in daily practice, efforts are being made to enable upload facilities; not only to increase the size of the database, but also its quality and the representativeness of the data for the country from which the data were obtained. These efforts will increase the potential value of the database and the number of research questions that METEOR has the capacity to answer, helping us to better understand the disease and its treatment in different geographic and clinical settings, and to improve outcomes for our patients.

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